UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,699	11/17/2003	Timothy J. Cunningham	53844-5021	5388

7590 07/31/2007

DRINKER BIDDLE & REATH LLP
One Logan Square
18th & Cherry Streets
Philadelphia, PA 19103-6996

EXAMINER	
HAYES, ROBERT CLINTON	
ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
07/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/714,699	CUNNINGHAM ET AL.	
	Examiner	Art Unit	
	Robert C. Hayes, Ph.D.	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/20/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I (claims 1-3 & 22) in the reply filed on 12/11/06 is acknowledged. It is noted that all other claims have been cancelled.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-2 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. For example, the current recitation of "a... peptide having...", alone, does not necessarily involve the hand of man. It is suggested that amending claim 1 to "an isolated neuron survival-promoting peptide...", etc. should obviate this rejection.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6 & 7 of U.S. Patent No. 6,262,024. Although the conflicting claims are not identical, they are not patentably distinct from each other because the peptide of SEQ ID NO: 3 of the '024 comprises the peptide of SEQ ID NO: 1 of the instant invention, in which the two cysteines of SEQ ID NO: 1 of the instant invention are included and represented in SEQ ID NO: 3 of '024 as Xaa (i.e., as it also relates to "variants thereof" or "conservative amino acid substitutions" in claims 1 & 2, respectively). Note that the recitation of "having" is interpreted as open claim language. Likewise the recitation "variant thereof" encompasses additional amino acids at either end of the peptide of SEQ ID NO: 1. In that claim 6 of '024 is directed to pharmaceutical compositions, claim 3 of the instant invention is also encompassed by '024.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 & 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The sole written description provided within the specification is the human CHEC-9 polypeptide of SEQ ID NO: 1, and a CHEC-9 variant polypeptide of SEQ ID NO: 2. In contrast, pages 12-13 of the specification describe "functional equivalent" peptides as those peptide molecules with "conservative amino acid substitutions", as illustrated on page 13. However, not a single amino acid substitution exists between SEQ ID NO: 1 and SEQ ID NO: 2 that is a "conservative amino acid substitution". Thus, no adequate written description is provided in the instant specification as to what structurally constitutes a genus of "variant" or "functional equivalent" peptides thereof, because the description of the single peptide of SEQ ID NO: 1, and the different peptide of SEQ ID NO: 2, by themselves, do not reasonably provide description of a representative number of species to show Applicants are in possession of the claimed genus of functional peptides. In other words, one skilled in the art cannot reasonably visualize or predict what critical amino acid residues would structurally characterize the genus of polypeptides encompassed by claims 1-2, especially based on the comparison of SEQ ID NO: 1 with SEQ ID NO: 2. Therefore, an invitation for others to discover a representative number of species with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics has not reasonably been provided within the instant specification. Thus, the written description requirements under 35 U.S.C. 112, first paragraph are not met. See MPEP 2163.

5. Claims 1-3 & 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated peptide consisting of SEQ ID NO: 1, or for kits comprising such a peptide, does not reasonably provide enablement for any structurally and functionally undefined "CHEC-9 peptide", or "variant thereof", or biologically functional equivalents thereof, or for kits "for treating an [undefined] neurodegenerative disorder". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

First, the name, "CHEC-9 peptide" (i.e., as it relates to claim 22), or "variant thereof", alone (e.g., as defined on pages 12-13 & 17-19 of the specification) encompasses random "insertions, deletions, or substitutions of amino acids", or any biologically "functional equivalent" polypeptide, which provides little structural characterization and no functional characteristics for knowing how to make and use the instant invention. The specification fails to define what specific amino acids are critical for any CHEC-9-related function, or what specific amino acid residues distinguish the CHEC-9 peptide of the instant invention from any different CHEC-9-related protein. In contrast, the skilled artisan would reasonably expect that random mutations to the protein of SEQ ID NO: 1 (i.e., as it especially relates to changing all 9 of the 9 amino acid residues of SEQ ID NO: 1; as it relates to claim 2) would result in inactive CHEC-9-related proteins. For example, Rudinger states on page 3 that "it is impossible to attach a unique significance to any residue in a sequence. A given amino acid will not by any means have the same significance in different peptide sequences, or even in different positions of the same sequence". Rudinger then states on page 6 that "the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must be

determined from case to case by painstaking experimental study". Therefore, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for a CHEC-9-related protein's function would prevent the skilled artisan from determining whether any random modification or mutation to the CHEC-9 peptide of SEQ ID NO: 1 could be made which retains the desired function of the instant invention, because any such random modification/ mutation manifested within a structurally undefined polypeptide would be predicted to adversely affect the three-dimensional conformation of the polypeptide, without requiring undue experimentation to determine otherwise.

Lastly, the specification only discloses increase survival of SY5Y neuroblastoma cells (i.e., tumor cells; page 8 & Figure 1 of the specification), and decreased macrophage/ microglial proliferation (e.g., Figures 3-4 & 6) after a cortical brain lesion. No specific populations of neurons that contain receptors responsive to CHEC-9 are disclosed. No guidance how to generically treat neurodegenerative diseases are provided within the instant specification. In contrast, in order to practice the full scope of the invention for claim 22, "treating a neurodegenerative disease" requires functional regeneration of the damaged axon; especially as it relates to neurodegenerative disorders where neurons otherwise die. Therefore, the minimal requirement for functional regeneration is that *de novo* axonal cell growth be completed for a sufficient distance to re-establish a proximity relationship to the prior target. Importantly, effective treatment requires functional regeneration (i.e., synaptogenesis). However, regeneration does not occur either because processes fail to grow the necessary distance, they are in competition with other nearby neuronal processes not derived from the affected nerve, astrocytic scarring blocks axonal elongation, or because of misdirected axonal growth (e.g., see

Jackowski, pgs. 309-310). In other words, neurons do not regenerate in the CNS (e.g., Jackowski, pg. 305, last *pp*). In contrast, the instant specification fails to provide any guidance on how to prevent damaged neurons from degenerating, or how to prevent any neuron from dying that is damaged, or how any "neurodegenerative disease", each with their unique etiology, can be effectively treated with any CHEC-9 peptide in the CNS in a kit; nor how to assay such *in vivo*.

Claim Rejections - 35 U.S.C. § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 & 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Cunningham et al. (IDS Ref # C; 2000).

Cunningham et al. teach a Y-P30 polypeptide "*having the sequence of*"/comprising SEQ ID NO: 1, "or variants thereof" (e.g. pg. 457, right column; as it relates to claim 1). Note that the recitation of "having" is interpreted as open claim language. Likewise the recitation "variant thereof" encompasses additional "conservative amino acids" at either end of the peptide of SEQ ID NO: 1 (i.e., as it relates to claims 1 & 2). In that Cunningham teach treating animals with this peptide in PBS and/or gelfoam (pg. 459), in which PBS and/or gelfoam are well known "biologically acceptable carriers"/ "vehicles for administration" for use in a kit, the limitations of claims 3 & 22 are met. In that the article of Cunningham et al itself reasonably constitutes

"instructions" for using the kit of claim 22 for "small bilateral lesions of cortical area 2", for example (e.g., Table 2), the remaining "optional" limitations of claim 22 are also anticipated.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (571) 272-0885. The examiner can normally be reached on Monday through Thursday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (571) 272-0841. The fax phone number for this Group is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert C. Hayes, Ph.D.
July 25, 2007

ROBERT C. HAYES, PH.D.
PRIMARY EXAMINER